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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,927	06/24/2003	Jean Merrill	USAV2001/0172USNP	1793
5487	7590	11/15/2006	EXAMINER	
ROSS J. OEHLER SANOFI-AVENTIS U.S. LLC 1041 ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807			XIE, XIAOZHEN	
			ART UNIT	PAPER NUMBER
			1646	
DATE MAILED: 11/15/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/602,927	Applicant(s) MERRILL ET AL.	
	Examiner Xiaozhen Xie	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 10 and 11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 10 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). B
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

Applicant's amendment of the claims received on 28 August 2006 has been entered. Applicant's remarks received on 28 August 2006 are acknowledged.

Election/Restriction

In the Office Action mailed 9 February 2006, Applicant was required to elect a restriction under 35 U.S.C. 121 from the following groups: (I) claims 1-6 are drawn to a method of modulating differentiation of oligodendrocytes; (II) claims 7-13 are drawn to a method of inducing remyelination at a site requiring remyelination; (III) claims 14-15 are drawn to a method of obtaining a molecule that induces migration of cells to a site requiring myelination; (IV) claims 16-17 are drawn to a method of obtaining a molecule that induces dedifferentiation of an oligodendrocyte or prevents differentiation of an oligodendrocyte precursor cell.

In a response received on 8 March 2006, Applicant elected Group II, claims 7-13, and amended claim 7 to depend from claim 1. Applicant argues that Groups I and II should be examined together. In a telephonic interview on 15 June 2006, Applicant was informed that since the non-final office action mailed 28 March 2006 technically examined the scope of the subject encompassed by claim 1, upon further review and consideration, the next office action would not be made final, and Groups I and II will be examined together.

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Claims 8, 9 and 12-17 have been cancelled. Claims 1-7, 10 and 11 are pending and under examination. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Objection Withdrawn

The objection of claim 7 for reciting nonelected invention is withdrawn for reasons set forth above.

Claim Rejections Maintained

The amended claims 7, 10 and 11 remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. This rejection also applies to the re-joined claims 1-6.

Applicant argues that the conclusion from Selvaraju et al. (Selvaraju) is not applicable because: (a) Applicant uses primary normal rat oligodendrocyte progenitors from neonatal rats, and Selvaraju used CG4 (rat) and Oli-neo (mouse) cell lines that are not normal, not oligodendrocyte progenitors, and not representative of primary oligodendrocyte phenotypically or functionally; (b) Applicant shows osteopontin (OPN) drive migration of primary oligodendrocyte progenitors from neonatal rats, and Selvaraju didn't show proliferation, migration or differentiation of purified oligodendrocyte progenitors in response to OPN; and (c) Applicant uses a different demyelinating and remyelinating model and concentrated on spinal cord while Selvaraju looked at brain.

Applicants' argument has been fully considered but has not been found to be persuasive.

First, Selvaraju used both in vitro oligodendrocytes differentiation and the in vivo remyelination model, the cuprizone model. For in vitro studies, Selvaraju used Oli-neu and CG-4 cell lines. Oli-neu cells are oligodendrocyte precursors (OLPs) (see pp. 711, right column, lines 1-5 in the 2nd paragraph), which have been well-characterized and further demonstrated in Selvaraju study for being suitable for myelination study in the nervous system (see Jung et al., 1995, Eur. J. Neurosci., 7:1245-1265). Similarly, rat CG-4 cells are also characterized as OLPs (pp. 712, right column, lines 7-9, and see Louis et al., 1992, J. Neurosci. Res., 31:193-204). Further, the in vivo cuprizone model study reflects OPN effects in oligodendrocytes and the precursor within a mammalian organism. Second, Selvaraju did show proliferation, migration or differentiation of purified oligodendrocyte progenitors in response to OPN. As stated in the previous office action, Selvaraju teaches that recombinant OPN induces proliferation of oligodendrocyte precursor cells (see pp. 711, right column, section *Recombinant OPN protein induces Oli-neu cellular proliferation*, and pp. 712, Fig. 5), and Selvaraju teaches recombinant OPN treatment stimulates differentiation (see pp. 713, left column, section *Recombinant OPN treatment stimulates myelin sheath formation in mixed cortical cultures*). Third, an experimental model and an assay are only means to test a hypothesis. Models/assays can be different, however, conclusion should be consistent, e.g., Northern blot and RT-PCR can both be used to measure an mRNA level. Applicant has not provided evidence that OPN-mediated regulation of oligodendrocyte precursors during myelination process is different, or opposite, in mechanism between spinal cord and brain. Since Selvaraju teaches a method of inducing differentiation of

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oligodendrocyte precursor cells and enhancing remyelination by increasing exposure of oligodendrocyte precursor cells to OPN, which is in contradiction to the method of the instant invention, and the specification has failed to provide any objective evidence or working examples, one skilled in the art would not know how to practice the claimed invention without undue experimentation.

Further, claims 2-5 recite reducing exposure of oligodendrocytes and precursors thereof to OPN by using an antibody that specifically binds to OPN, or by inactivating OPN receptor with an OPN antagonist or an antibody, and claim 6 recites modulating the activity of a receptor for OPN. The specification, however, fails to teach such antibody or how to inactivate or modulate the OPN receptor using said agents. The specification discloses on pp. 33 that the receptor-inhibiting molecule can be any molecule, a peptide, carbohydrate, organic molecule or combination thereof, and that an OPN antibody can be found to activate the OPN receptor (pp. 27, lines 5-19). There is no teaching in the specification as to how to make and use these agents. Clearly, it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

Due to the large quantity of experimentation necessary to determine how to modulate differentiation of oligodendrocytes and enhance remyelination by reducing exposure of oligodendrocytes and precursors to OPN, or by first increasing exposure of oligodendrocyte precursor cells to OPN, then reducing the exposure to OPN, using unidentified molecules or antibodies, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the

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complex nature of the invention, the state of the prior art establishing that OPN stimulates differentiation and remyelination of oligodendrocytes, and the breadth of the claim which fails to recite particular activities and structure features for antagonists and antibodies etc., undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

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Conclusion

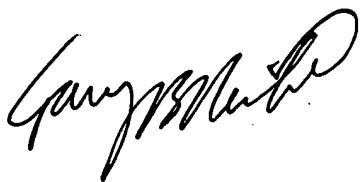
NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
November 9, 2006



GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600